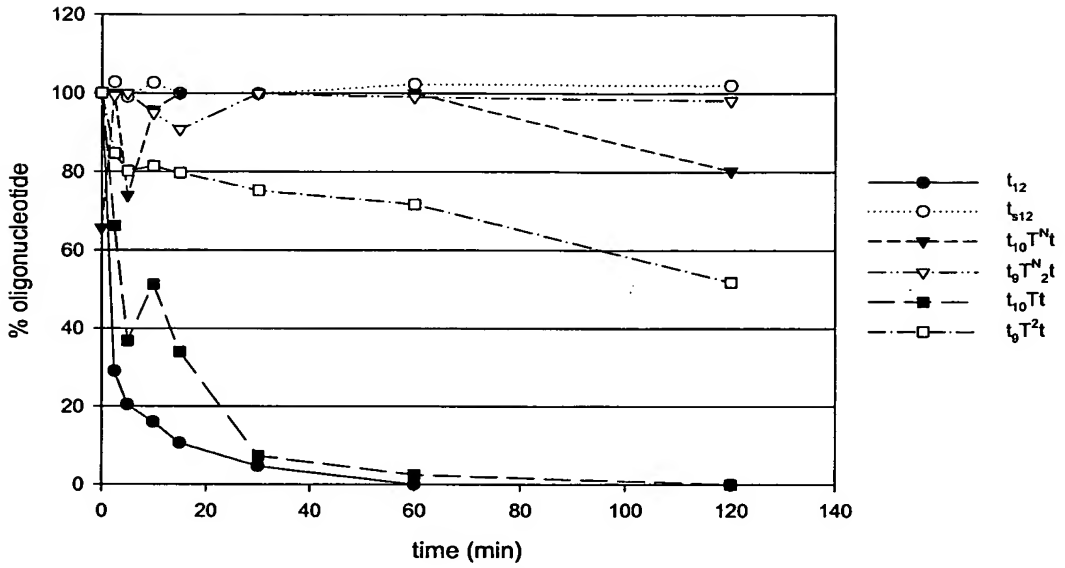

Fig 1

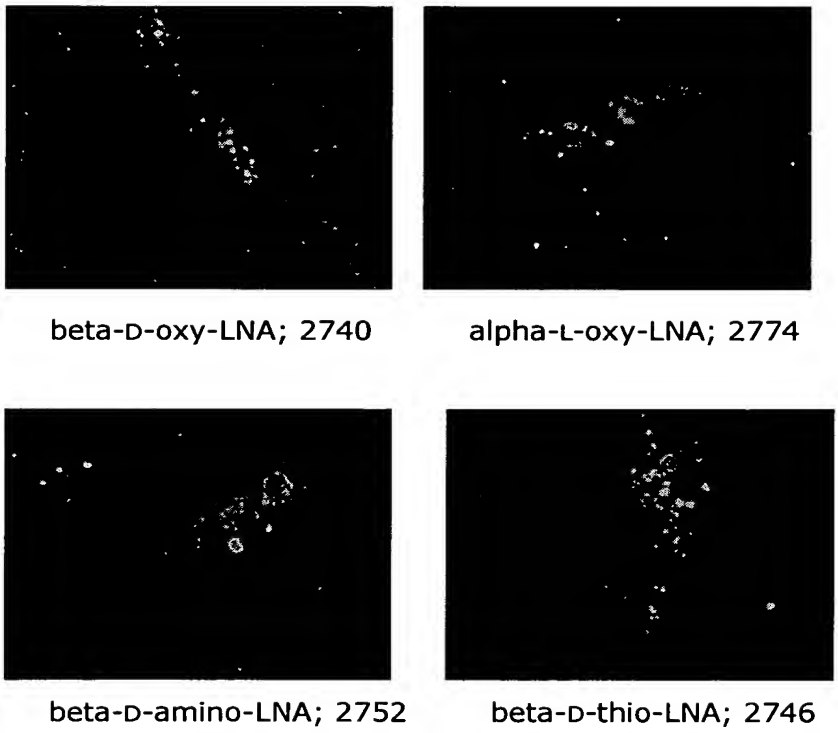

Fig 2

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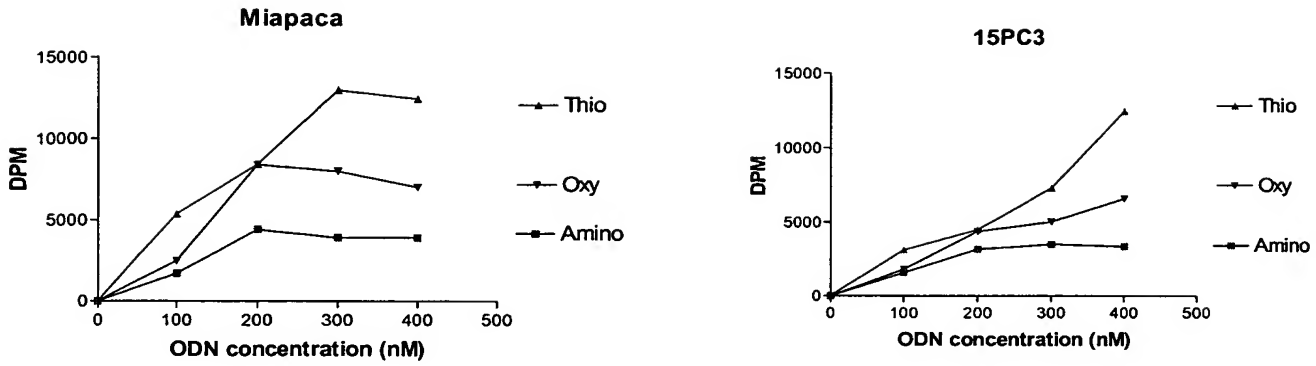

Miapaca
15000
10000
5000
0
DPM
0
100
200
300
400
500
ODN concentration (nM)
Thio
Oxy
Amino
15PC3
15000
10000
5000
0
DPM
0
100
200
300
400
500
ODN concentration (nM)
Thio
Oxy
Amino

Fig 3

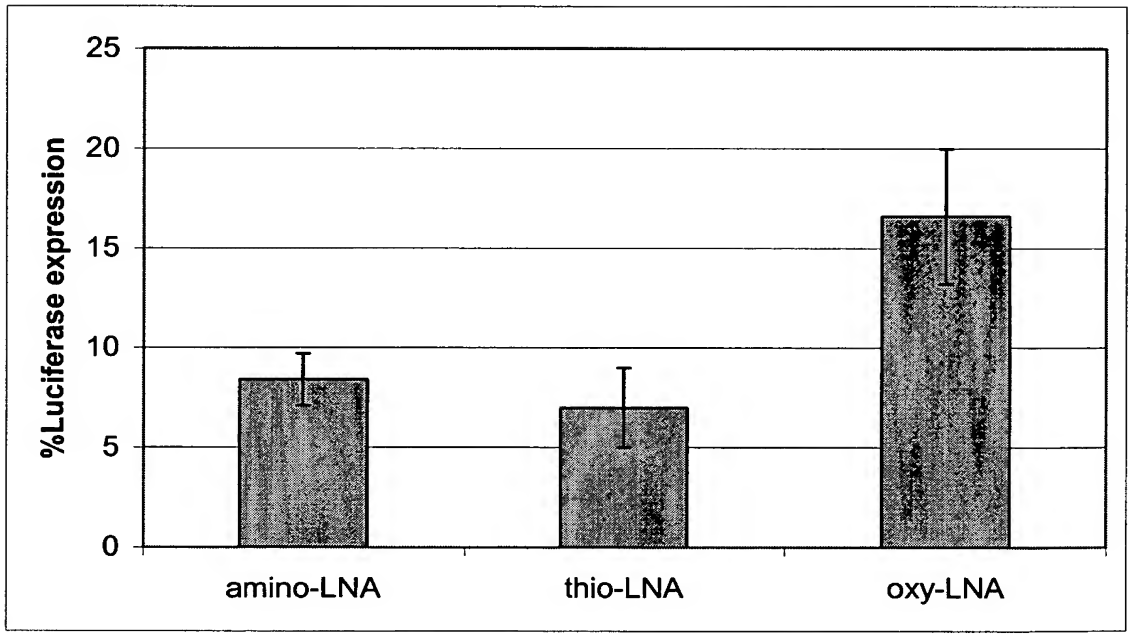
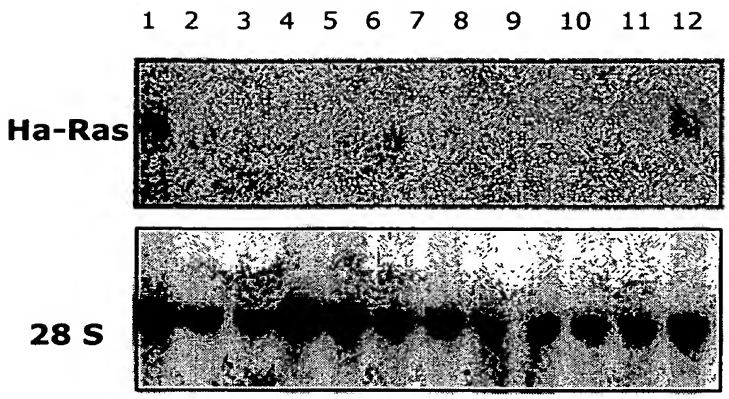
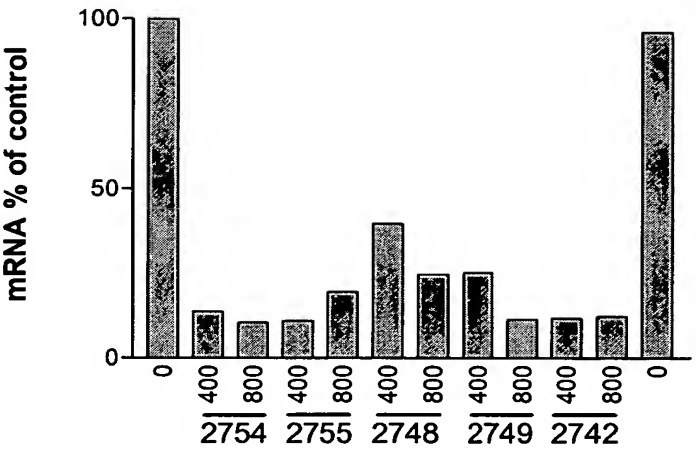

25
20
15
10
5
0
%Luciferase expression
amino-LNA
thio-LNA
oxy-LNA

Fig 4





1= mock control transfection
2=400nM 2754
3=800nM 2754
4=400nM 2755
5=800nM 2755
6=400nM 2748
7=800nM 2748
8=400nM 2749
9=800nM 2749
10=400nM 2742
11=800nM 2742
12= mock control transfection

Fig 5

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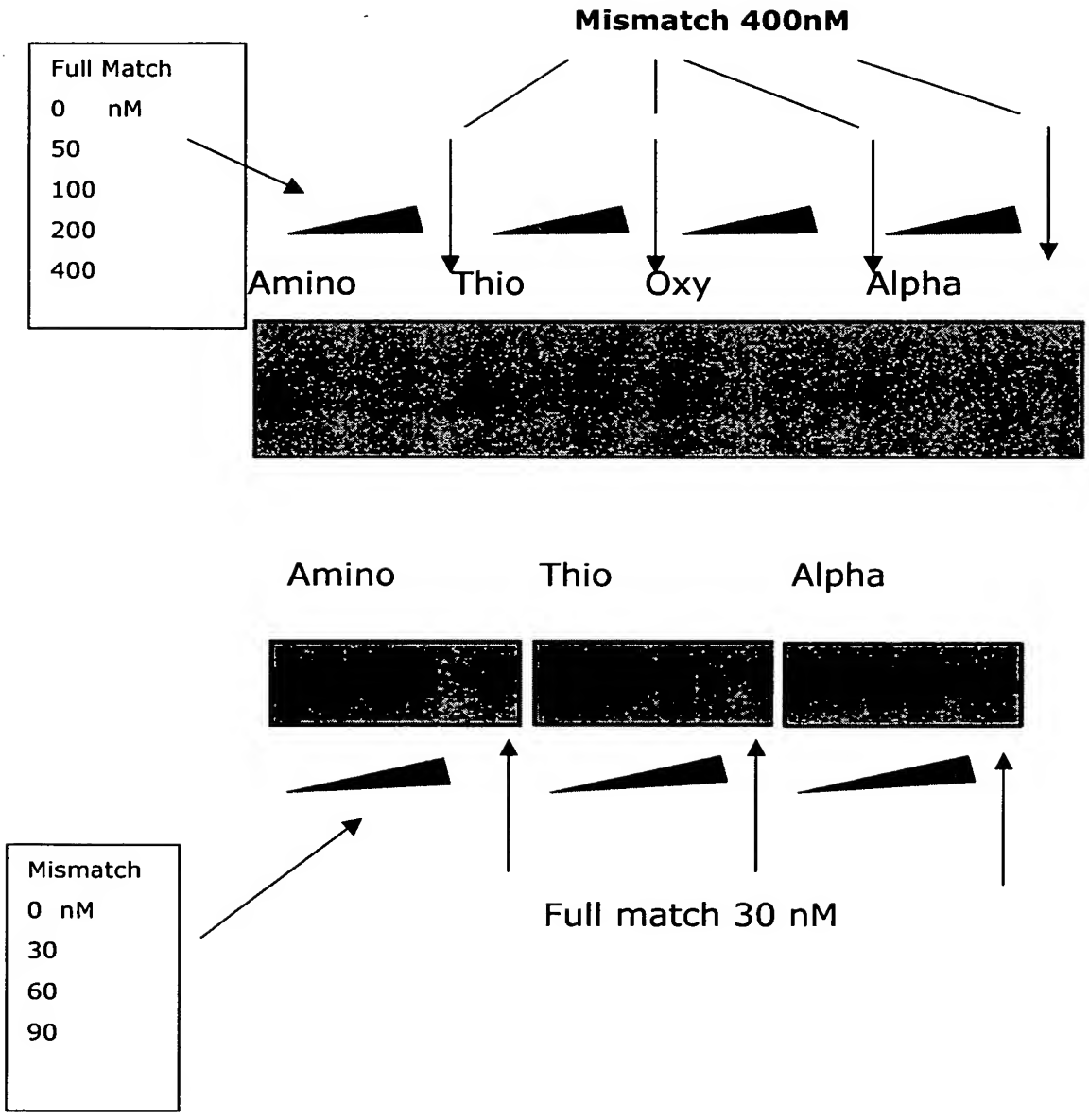

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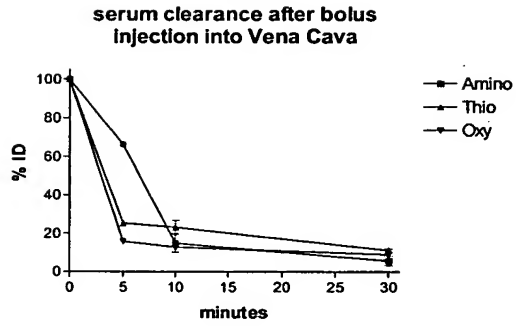
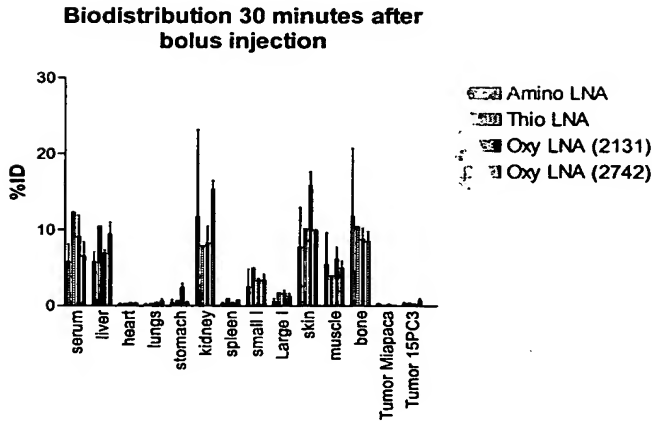
lane	input	Ha-Ras	28S		%Ha-Ras
1	mock	1295	341598	0,003791	100
2	5nm 2754	579	314264	0,001842	37,33333
3	10nm 2754	191	264155	0,000723	14,65168
4	20nm 2754	149	346839	0,00043	8,705048
5	40nm 2754	142	358302	0,000396	8,030673
6	20nm 2756	1082	389683	0,002777	56,26375
13	mock	2038	331165	0,006154	100
14	5nm 2742	386	276874	0,001394	28,24997
15	10nm 2742	250	259534	0,000963	19,51905
16	20nm 2742	182	369254	0,000493	9,987551
17	40nm 2742	227	392719	0,000578	11,71269
18	20nm 2744	1069	480037	0,002227	45,12486
19	mock	1534	466543	0,003288	100
20	5nm 2776	364	474676	0,000767	15,53878
21	10nm 2776	167	519707	0,000321	6,511346
22	20nm 2776	53	411881	0,000129	2,607456
23	40nm 2776	105	375591	0,00028	5,664831
24	20nm 2778	703	184089	0,003819	77,38207

Fig 6


serum clearance after bolus injection into Vena Cava
% ID
minutes
Amino
Thio
Oxy


Biodistribution 30 minutes after bolus injection
%ID
Amino LNA
Thio LNA
Oxy LNA (2131)
Oxy LNA (2742)
serum
liver
heart
lungs
stomach
kidney
spleen
small I
Large I
skin
muscle
bone
Tumor Miapaca
Tumor 15PC3

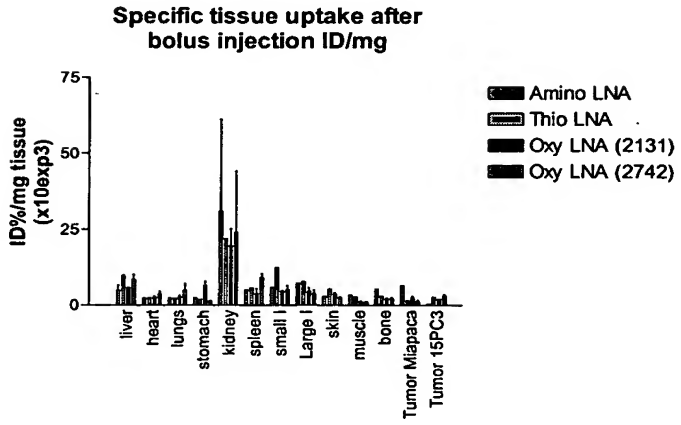
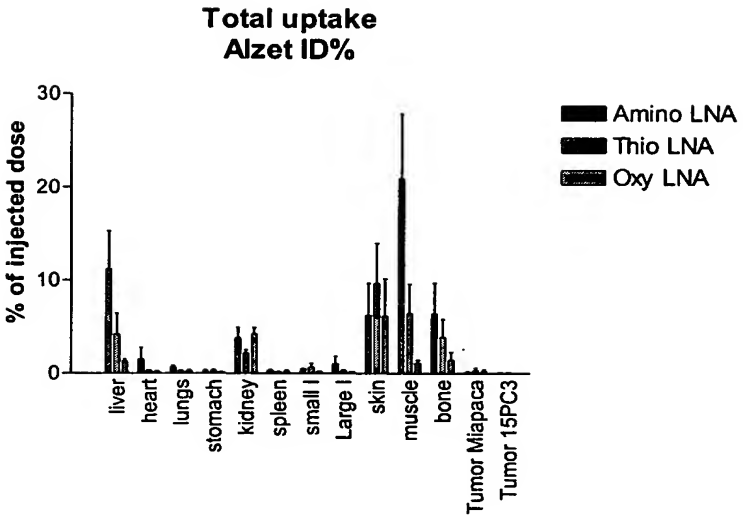

Specific tissue uptake after bolus injection ID/mg
ID%/mg tissue (x10exp3)
Amino LNA
Thio LNA
Oxy LNA (2131)
Oxy LNA (2742)
liver
heart
lungs
stomach
kidney
spleen
small I
Large I
skin
muscle
bone
Tumor Miapaca
Tumor 15PC3

Fig 7


Total uptake
Alzet ID%
% of injected dose
30
20
10
0
liver
heart
lungs
stomach
kidney
spleen
small I
Large I
skin
muscle
bone
Tumor Miapaca
Tumor 15PC3
Amino LNA
Thio LNA
Oxy LNA

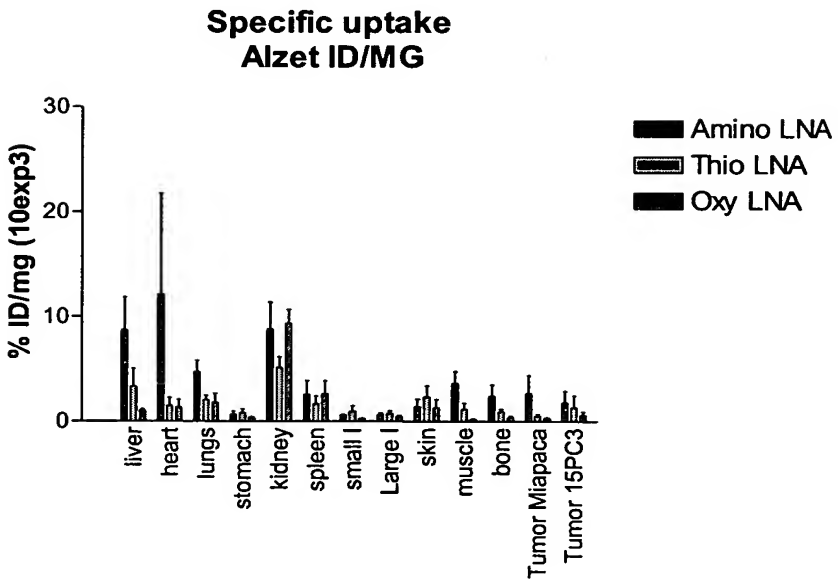

Specific uptake
Alzet ID/MG
% ID/mg (10exp3)
30
20
10
0
liver
heart
lungs
stomach
kidney
spleen
small I
Large I
skin
muscle
bone
Tumor Miapaca
Tumor 15PC3
Amino LNA
Thio LNA
Oxy LNA

Fig 8

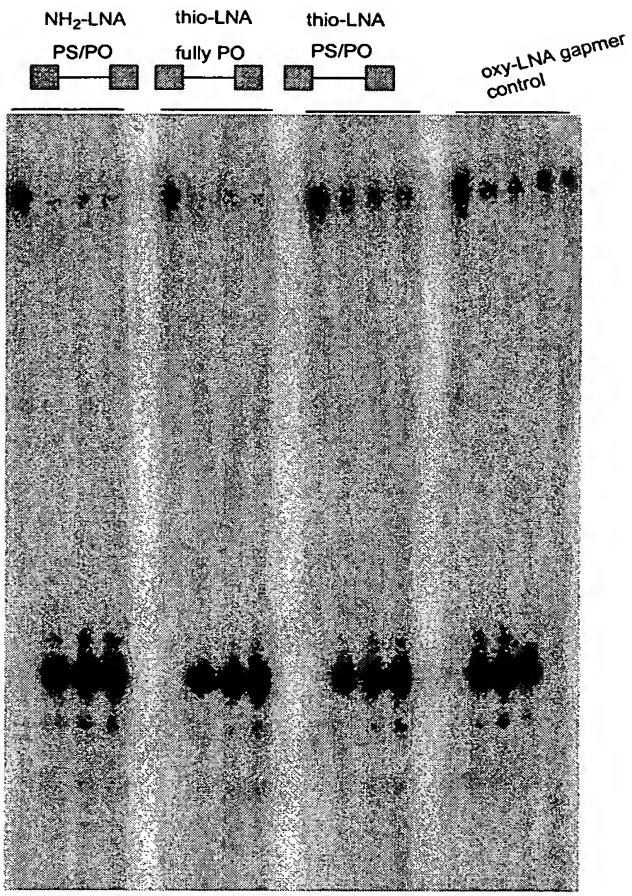


Fig 9

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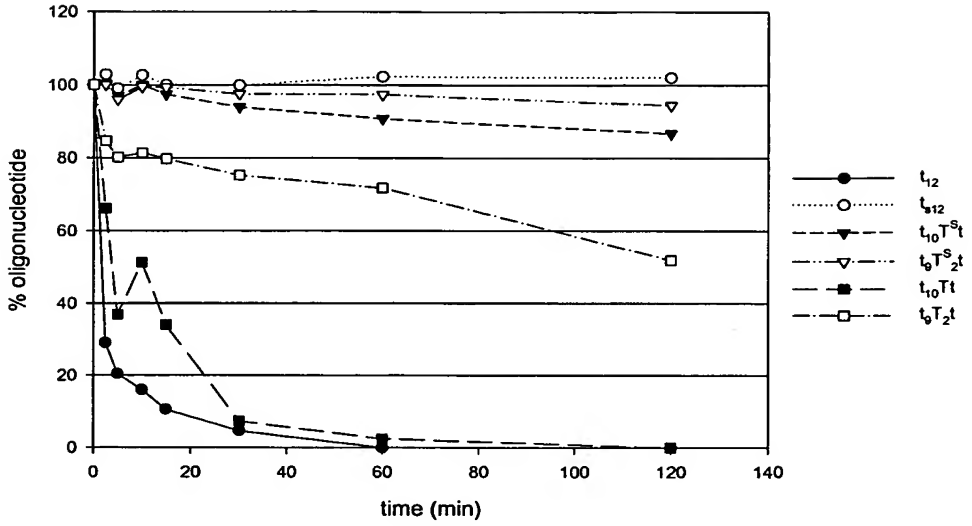
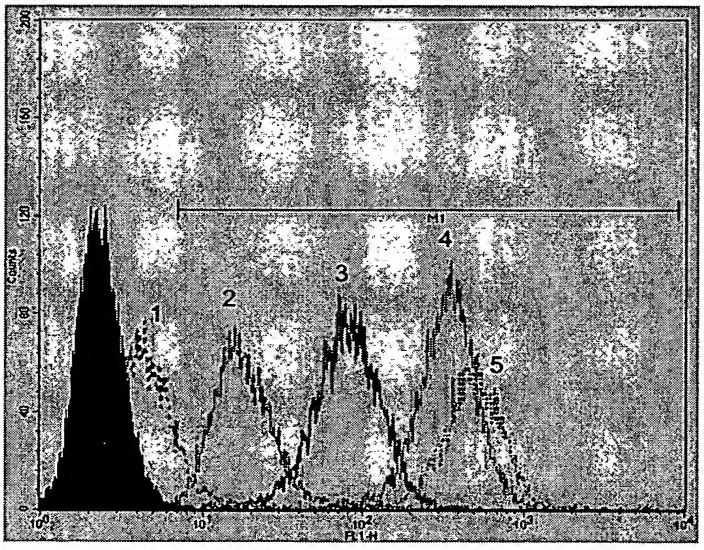


Fig 10



1. DNA/PO

2. oxy-LNA PS-gap/PO-flanks

3. thio-LNA all-PO

4. thio-LNA PS-gap/PO-flanks

5. DNA/PS

Fig 11

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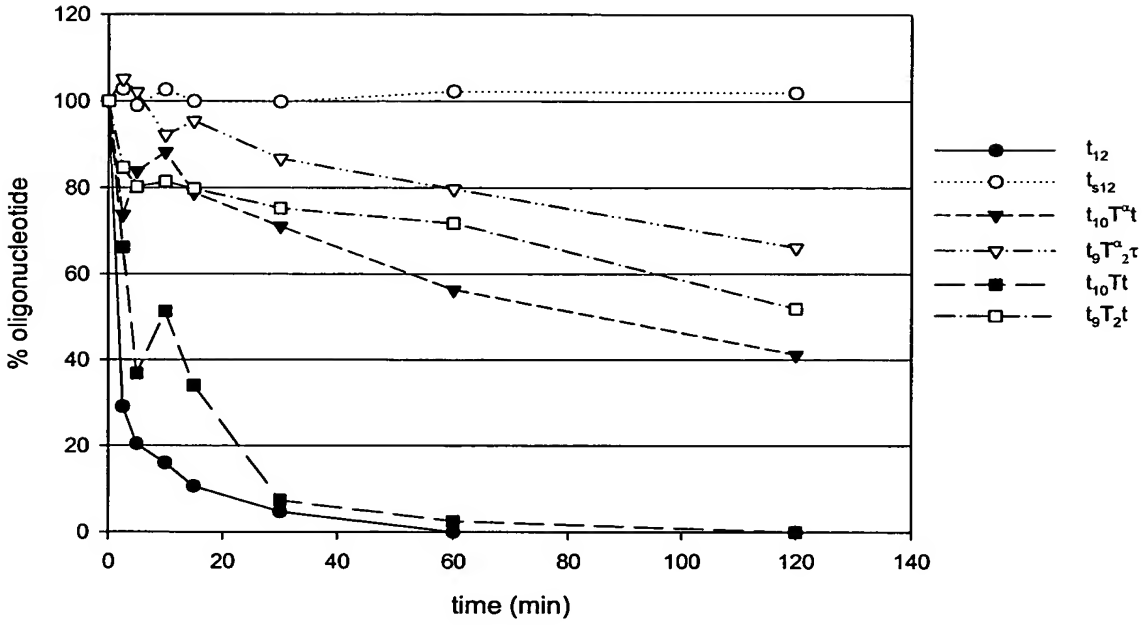
120
100
80
60
40
20
0
% oligonucleotide
0
20
40
60
80
100
120
140
time (min)
t_{12}
t_{s12}
$t_{10}T^{\alpha}t$
$t_9T^{\alpha}{}_2\tau$
$t_{10}Tt$
t_9T_2t

Fig 12

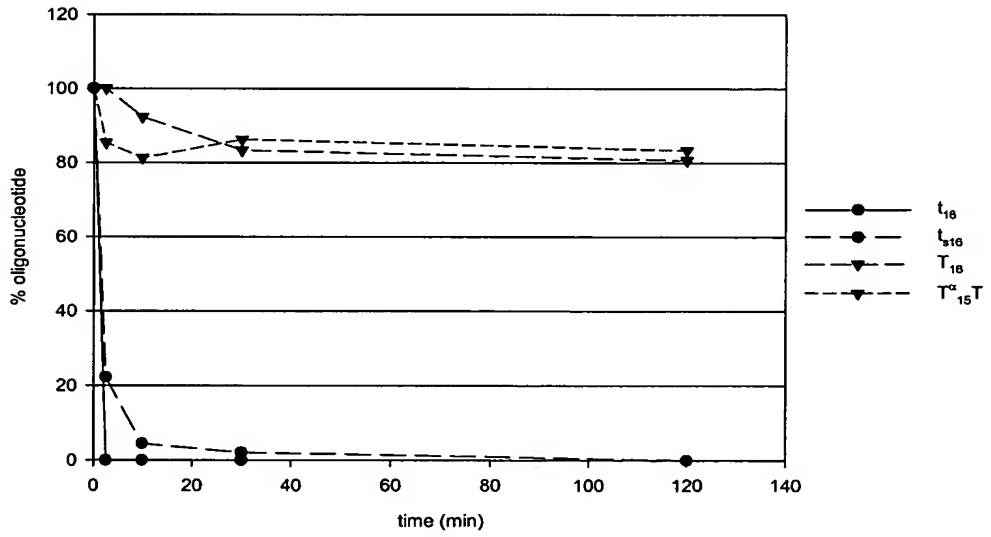
120
100
80
60
40
20
0
% oligonucleotide
0
20
40
60
80
100
120
140
time (min)
t_{16}
t_{s16}
T_{16}
$T^{\alpha}{}_{15}T$

Fig 13

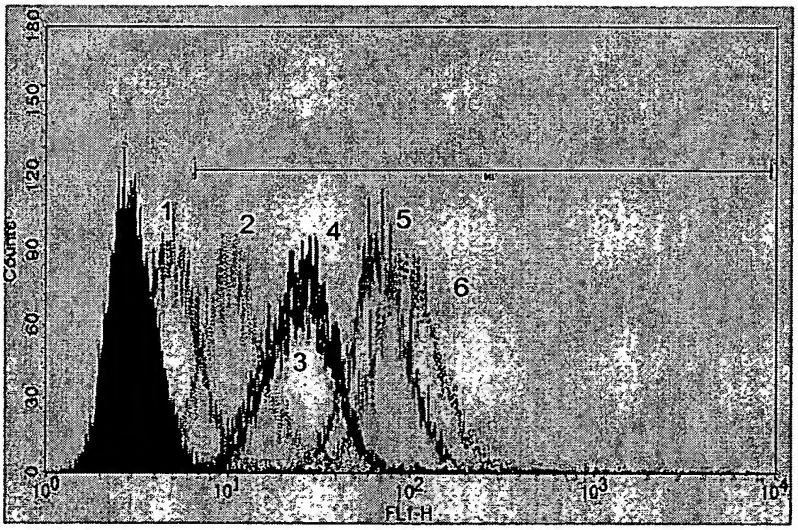

Fig 14

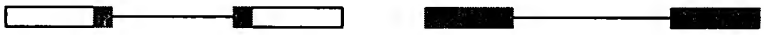

Fig 15

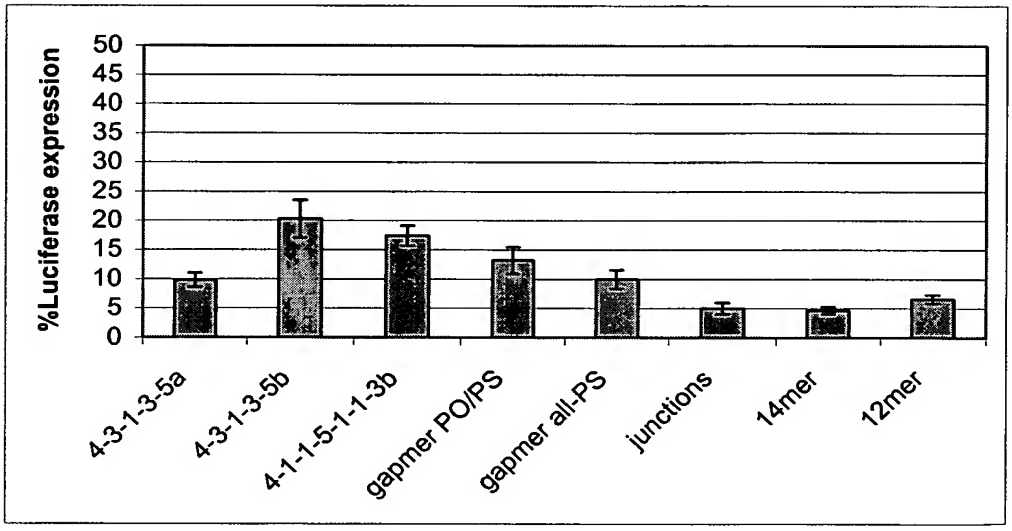

Fig 16

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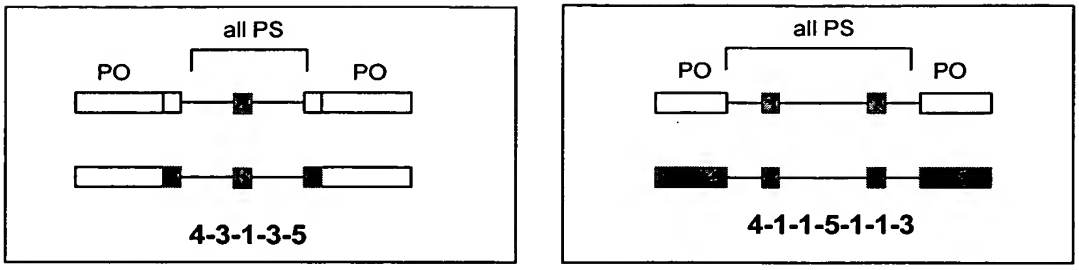
all PS
PO
PO
4-3-1-3-5
all PS
PO
PO
4-1-1-5-1-1-3

Fig 17

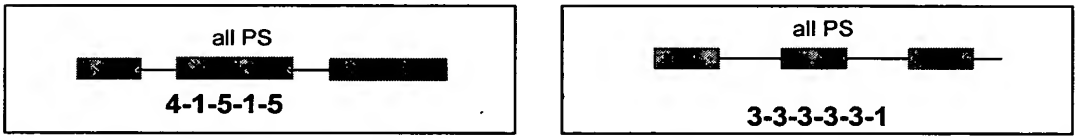
all PS
4-1-5-1-5
all PS
3-3-3-3-3-1

Fig 18

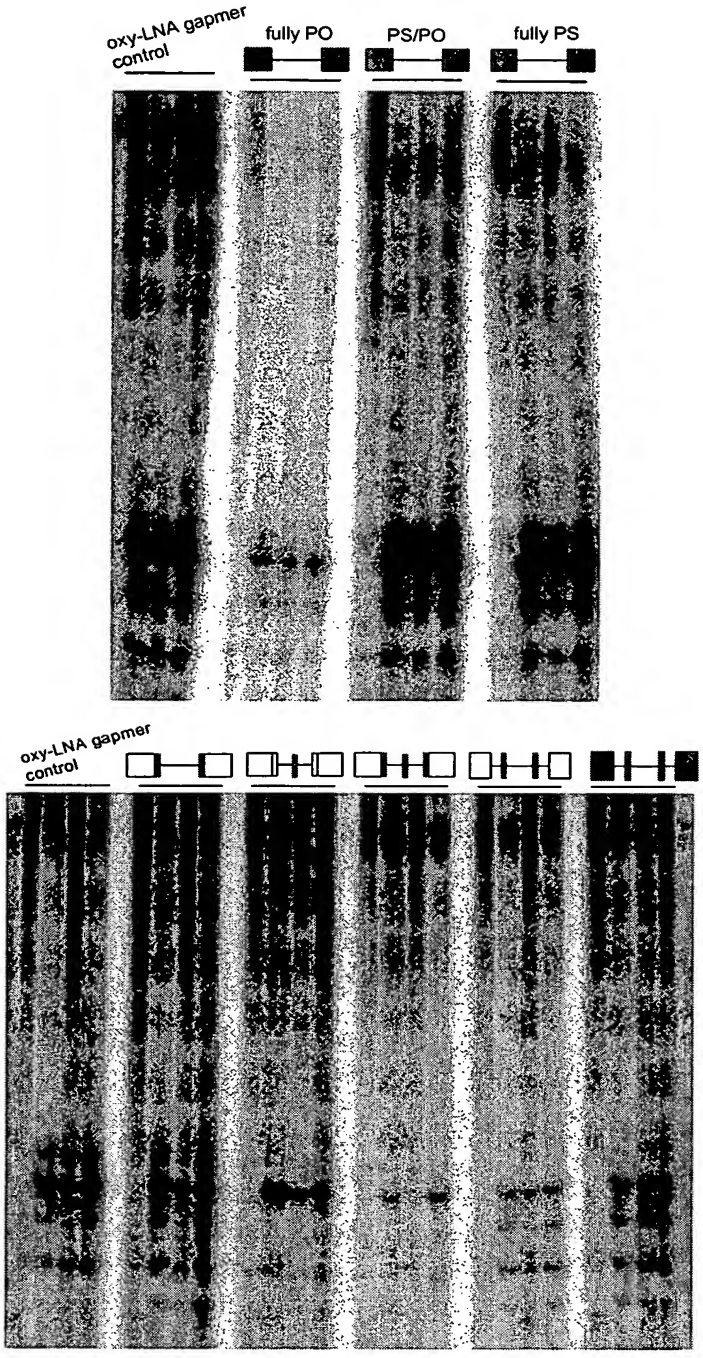

Fig 19

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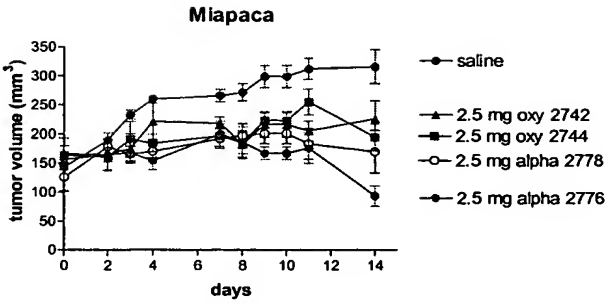
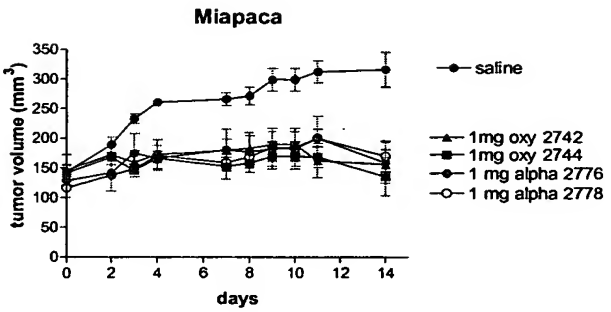
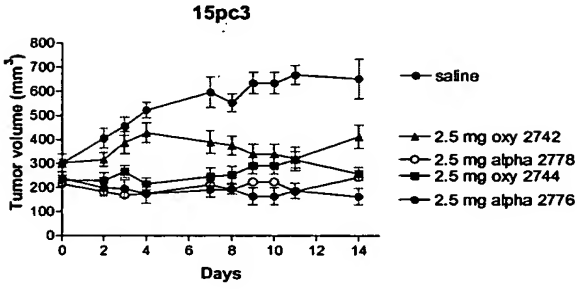

Miapaca
tumor volume (mm3)
days
saline
2.5 mg oxy 2742
2.5 mg oxy 2744
2.5 mg alpha 2778
2.5 mg alpha 2776


Miapaca
tumor volume (mm3)
days
saline
1mg oxy 2742
1mg oxy 2744
1 mg alpha 2776
1 mg alpha 2778


15pc3
Tumor volume (mm3)
Days
saline
2.5 mg oxy 2742
2.5 mg alpha 2778
2.5 mg oxy 2744
2.5 mg alpha 2776

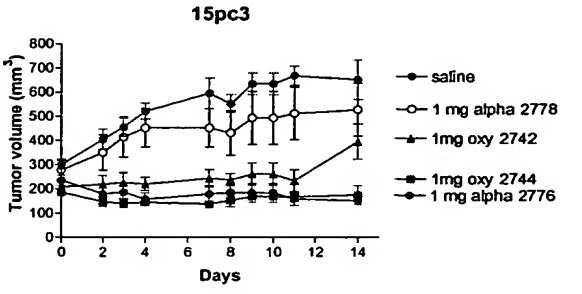

15pc3
Tumor volume (mm3)
Days
saline
1 mg alpha 2778
1mg oxy 2742
1mg oxy 2744
1 mg alpha 2776

Fig 20

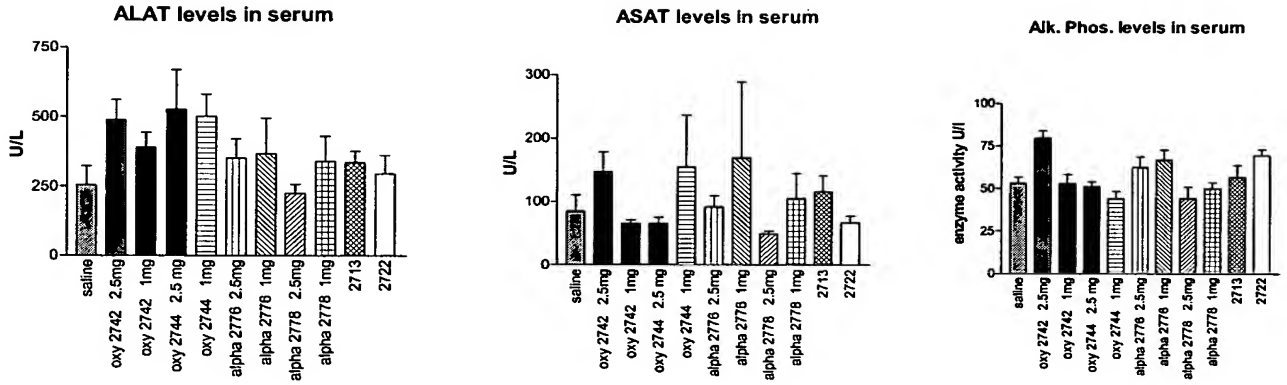


Fig 21

Group 1	saline	
Group 2	2.5 mg	2742
Group 3	1 mg	2742
Group 4	2.5 mg	2744
Group 5	1 mg	2744
Group 6	2.5 mg	2776
Group 7	1 mg	2776
Group 8	2.5 mg	2778
Group 9	1 mg	2778
Group 10	5 mg	2713
Group 11	5 mg	2722

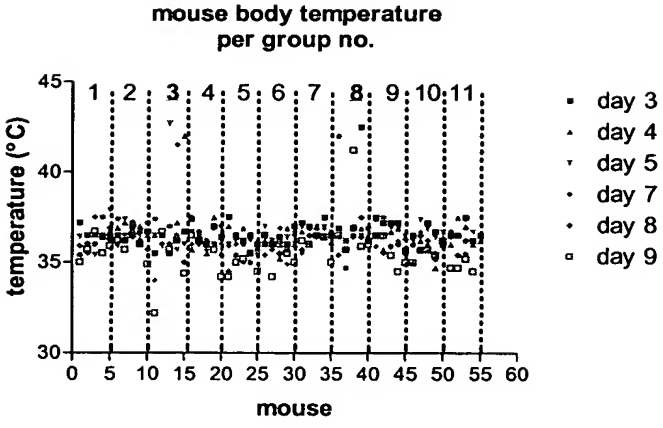


Fig 22

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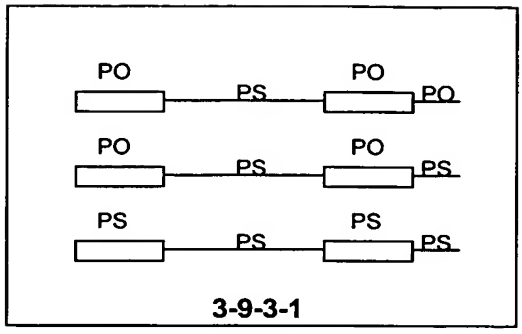

Fig 23

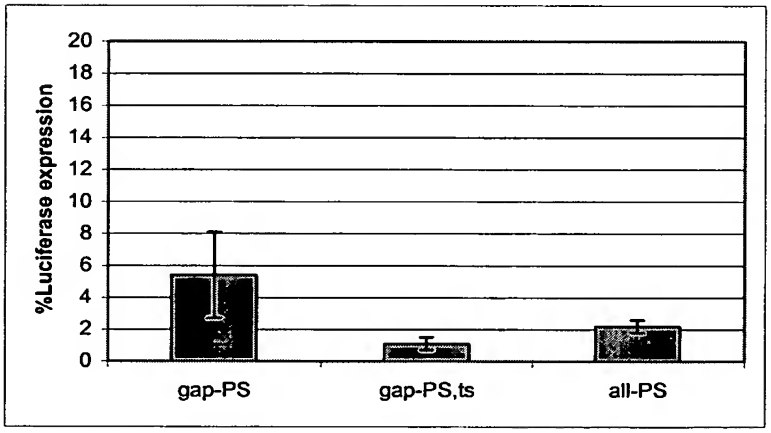

Fig 24

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